REMARKS

Claim 4 is pending. Claims 37-44 have been added. Support for the recitation of "embryonic" in claim 37 can be found at least at page 8, lines 6-12.

Support for new claim 38 can be found at least in original claim 4 which has language identical to new claim 38. Thus, the subject matter of original claim 4 is being added back to the application as a new claim as discussed in the interview of October 20, 2003 with Examiner Woitach.

New claims 39-41 add the limitation that the cell stains positive for the SSEA-1 antigen and claims 42-44 add the limitation that the cell stains positive for the SSEA-1 antigen and stains positive for alkaline phosphatase. Support for these limitations can be found at least at page 18, lines 28-31, and page 18, lines 26-28, respectively.

INTERVIEW

Examiner Woitach kindly agreed to an interview which was conducted on October 20, 2003. Present at this interview were David Perryman and David Huizenga representing Applicant. During this interview the remaining issues in the outstanding office action were discussed. It was agreed that Applicant would (1) address the issues regarding the method used in Donovan et al., Nature 414:92-97 (2001), to produce the pluripotential embryonic stem cells from primordial germ cells by providing evidence of a nexus between the method taught in the present application with the data discussed in Donovan et al., and (2) Applicant would address arguments related to EC cell differentiation in monolayer culture. The likelihood of an interference with United States Patent 6,200,806 was discussed. It was agreed that there was overlapping subject matter and that Applicant would submit a Request for Interference under 37 C.F.R. § 1.607. It was also agreed that Applicant could add back the language "embryonic" into a new claim, so that the claim was specifically drawn to "pluripotent embryonic stem cells."

REJECTION UNDER 35 U.S.C. § 112

Claim 4 stands rejected under 35 U.S.C. § 112, first paragraph, on the basis that the specification, while being enabling for a non-murine mammalian pluripotential cell, allegedly does not provide enablement for such a cell having a normal karyotype.

As discussed during the interview of October 20, 2003, Donovan et al. states, "Three types of mammalian pluripotent stem cell lines have been isolated – embryonal carcinoma (EC) cells, the stem cells of testicular tumors; embryonic stem (ES) cells, derived from pre-implantation embryos; and embryonic germ (EG) cells derived from primordial germ (PGC) cells of the post-implantation embryo." Donovan et al., p. 92. Donovan et al. is choosing to discuss ES and EG cells in terms of where the starting cell is derived, but indicates that their end properties of pluripotency and differentiation capabilities are the same. Table 1 of Donovan et al. indicates that cells derived from PGC cells (EG) and cells derived from pre-implantation blastocysts are both euploid as discussed in the interview.

The Office Action alleges (1) that it would have been unpredictable to obtain the claimed cells because the production of stem cells, as evidenced by Piedrahita et al., Theriogenology 34:879-901 (1990), is allegedly unpredictable from species to species, and (2) that there is no nexus between the evidence of human pluripotent stem production disclosed in Donovan et al. and the methods of pluripotent embryonic stem cell production disclosed in the present application.

First, it is axiomatic that only a single method of enabling a claim is required. As long as there is at least a single method disclosed for producing the cells of claims 4 and 37-44 that works, production of the cells is enabled. In such a case, unpredictability of other methods is not relevant.[1] As disclosed in the present application the disclosed methods can be used with epiblast cells and embryonic ectoderm which includes blastocysts and can include pre-implantation blastocyst as well as primordial germ cells. (Page 8, lines 4-5, of the present application, for example). Cells produced by this method from these various sources are encompassed by the present claims. Piedrahita et al. and Cruz et al., Origin of Embryonic and Extraembryonic Cell Lineages in Mammalian Embryos *in* Animal Applications of Research in Mammalian Development, pages 147-204 (Cold Spring Harbor Laboratory Press, 1991), focus on a method of isolation different than that disclosed in the present application. Therefore,

Piedrahita et al. and Cruz et al. are not relevant to the predictability of the method disclosed in the present application which enables claims 4 and 37-44.

Applicant has cited data in Donovan et al. showing that ES and EG cells have a euploid karyotype (see, for example, Table 1, page 93). With respect to whether there is a nexus between the results disclosed in Donovan et al., as discussed in the interview of October 20, 2003, Donovan et al. states (Box 1 on page 94): "Both human and mouse EG cells can be derived using the same combination of factors, suggesting that some of the mechanisms regulating the development of the germ line have been conserved during mammalian evolution." In support of this, Donovan et al. cites among others, Matsui Y, Zsebo K, and Hogan BL., "Derivation of pluripotential embryonic stem cells from murine primordial germ cells in culture," Cell 70(5):841-7 (1992) [reference 13], which was the publication which formed in part the basis of the present application. This provides the nexus between the data in Donovan et al., showing that the claimed cells will be euploid and the methods used to produce that data, and the methods disclosed in the present application.

Therefore, Applicant has clearly enabled human pluripotential stem cells having a normal karyotype and withdrawal of the rejection is respectfully requested.

Applicant notes with appreciation the indication in the Office Action that claim 4 is free of the art. Applicant notes that Claim 37 is also free of the art. In addition, Claim 38 is patentable over embryonic carcinoma art at least because of the recitation "give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture" in this claim. Embryonic carcinoma cell lines do not differentiate into multiple phenotypes in monolayer culture, without the addition of exogenous factors. As evidence of this, Applicant submits with this Amendment Appendix C (available at http://stemcells.nih.gov/stemcell/pdfs/appendixc.pdf) of "Stem Cells: Scientific Progress and Future Research Directions" (available at http://stemcells.nih.gov/stemcell/scireport.asp) from the National Institute of Health's website dedicated to stem cells (http://stemcells.nih.gov/index.asp). On page 9, column 1, third

[1] Applicant notes the present claims still cover cells having the claimed characteristics that are made by other methods. Only one enabled method for making the claimed cells is needed for enablement, but this does not limit

paragraph, of Appendix C, the authors note that ES cells begin to differentiate spontaneously and form embryoid bodies when grown at high densities, but then state that "human EC cells remain undifferentiated when grown at high densities."

Pursuant to the above amendments and remarks, reconsideration and allowance of the pending application is believed to be warranted. The Examiner is invited and encouraged to directly contact the undersigned if such contact may enhance the efficient prosecution of this application to issue.

A Credit Card Payment Form PTO-2038 authorizing payment in the amount of $1125.00, representing $740.00 for the fee for a small entity under 37 C.F.R. § 1.17(a)(4) and $385.00 for the fee for a small entity under 37 C.F.R. § 1.17(e), a Request For Continued Examination Under 37 C.F.R. § 1.114, a Supplemental Information Disclosure Statement, a Request For Interference Pursuant To 37 C.F.R. §§ 1.604 And 1.607, and a Request For A Four-Month Extension Of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

NEEDLE & ROSENBERG, P.C.

David G. Perryman
Registration No. 33,438

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the scope of the claims to cells made by that method.

CERTIFICATE OF EXPRESS MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as Express Mail, Label No. El 9920 18835 US, in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date indicated below.

Phillip A. Van Gelder — June 1, 2004

Phillip A. Van Gelder — Date

ATTORNEY DOCKET NO. 16016.0005US
PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	)	
	)	
Hogan, Brigid L.M.	)	Art Unit: 1632
	)	
Application No. 08/813,829	)	Examiner: Woitach, Joseph
	)	
Filing Date: March 6, 1997	)	Confirmation No. 3939
	)	
For: STEM CELLS AND METHOD OF MAKING SAME	)	

REQUEST FOR INTERFERENCE PURSUANT TO 37 C.F.R. §§ 1.604 AND 1.607

Mail Stop RCE
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450
Attn. Examiner Joseph Woitach,
Art Unit 1632

NEEDLE & ROSENBERG, P.C.
Customer Number 23859

Sir:

Please consider the following Request for an Interference filed under 37 C.F.R. §§ 1.604 and 1.607.

Claim 4 is pending. Submitted with this Request For Interference is an Amendment and Response to Office Action, a Request For Continued Examination Under 37 C.F.R. § 1.114, a Supplemental Information Disclosure Statement will be submitted, and a Request For A Four-Month Extension Of Time. The claims pending in this application, upon entry of the accompanying Amendment, are set forth in Appendix I attached hereto. Support for claims 37-44 can be found throughout Applicant's specification as illustrated in Appendix II attached hereto. Appendix III contains a comparison of claim 1 of the '806 patent and claim 4 of the present application. Appendix IV contains the claims issued in United States Patents 6,200,806 and 5,843,780 and the claims of published United States Patent Applications 09/982,637 and 09/761,289.

In accordance with the provisions of 37 C.F.R. § 1.604, Applicant requests that an interference be declared between this application and U.S. Patent Application Nos. 09/982,637 (the '637 application) and 09/761,289 (the '289 application).

In accordance with the provisions of 37 C.F.R. § 1.607, Applicant requests that an interference be declared between this application and unexpired U.S. Patent No. 6,200,806 (the '806 patent) and U.S. Patent No. 5,843,780 (the '780 patent).

A. Summary of the Interview with Examiner Woitach

Examiner Woitach kindly agreed to an interview which was conducted on October 20, 2003. Present at this interview were David Perryman and David Huizenga representing Applicant. During this interview the remaining issues in the outstanding office action were discussed. It was agreed that Applicant would (1) address the issues regarding the method used in Donovan et al., Nature 414:92-97 (2001), to produce the pluripotential embryonic stem cells from primordial germ cells by providing evidence of a nexus between the method taught in the present application with the data discussed in Donovan et al., and (2) Applicant would address arguments related to EC cell differentiation in monolayer culture. The likelihood of an interference with United States Patent 6,200,806 was discussed. It was agreed that there was overlapping subject matter and that Applicant would submit a Request for Interference under 37 C.F.R. § 1.607. It was also agreed that Applicant could add back the language "embryonic" into a new claim, so that the claim was specifically drawn to "pluripotent embryonic stem cells."

B. Requirements of 37 C.F.R. § 1.607(a)(1)-(a)(6)

In accordance with 37 C.F.R. § 1.607(a)(1)-(a)(6), Applicant offers the following:

1. Requirement of 37 C.F.R. § 1.607(a)(1)

The patents at issue are U.S. Patent 6,200,806, issued March 13, 2001 (the "'806 patent") and U.S. Patent No. 5,843,780, issued December 1, 1998, (the "'780 patent"). The'806 and '780 patents on their face are assigned to the Wisconsin Alumni Research Foundation.

2. Requirement of 37 C.F.R. § 1.607(a)(2)

The proposed count is as follows: Claim 4 of the present application, claim 37 of the present application, or claim 38 of the present application. The text of the proposed count is:

An isolated human pluripotential stem cell which can:

(a) be maintained on feeder layers for at least 20 passages; and

(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture, wherein the cell has a normal karyotype;

or

An isolated human pluripotential embryonic stem cell which can

(a) be maintained on feeder layers for at least 20 passages; and

(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture, wherein the cell has a normal karyotype;

or

An isolated human pluripotential embryonic stem cell which can

(a) be maintained on feeder layers for at least 20 passages; and

(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture.

3. Requirement of 37 C.F.R. § 1.607(a)(3)

Claims 1-8 and claim 11 of the '780 patent and claims 1-8 and claim 11 of the '806 patent correspond to the proposed count. (Appendix IV)

4. Requirement of 37 C.F.R. § 1.607(a)(4)

Claims 4 and 37-44 of the present application correspond to the proposed count.

Claims 4, 37, and 38 of the present application correspond exactly to the proposed Count.

According to MPEP 2309.02 a claim corresponds to a Count "if, considering the Count as prior art, the claim would be unpatentable over the Count under 35 U.S.C. 102 or 35 U.S.C. 103."

Claims 1-8 and 11 of the '806 patent do not correspond exactly to the proposed Count, but should still correspond to the Count because if the Count was prior art to the claims, claims 1-8 of the '806 patent would be unpatentable over the Count under 35 U.S.C. 102 or 103. As discussed below, claim 1 of the '806 patent and claim 4 of the present application are the same patentable subject matter (see Section D, below, and Appendix III). Furthermore, none of the limitations in claims 2-8 of the '806 patent make them patentably distinct over the Count. The limitations of claims 2-8 of the '806 patent merely set forth inherent characteristics shared by the cells of Count. Inherent characteristics do not make a claim separately patentable. Lastly, claim 11 of the '806 patent is a product by process claim. The cells of claim 11 are cells encompassed by claim 1. For a product by process claim to be patentable the product itself must be patentable. Claim 11 cannot be patentable over claim 1 as these cells are the cells produced by the method of claim 9.

Claims 1-8 and claim 11 of the '780 patent do not correspond exactly to the proposed Count, but should still correspond to the Count because if the Count was prior art to the claims, claims 1-8 and claim 11 of the '780 patent would be unpatentable over the Count under 35 U.S.C. 102 because claims 1-8 and claim 11 of the '780 patent are drawn to primate embryonic stem cells, rather than the human embryonic stem cells of the Count, such as claim 4 of the present application. The Count, drawn to human pluripotent stem cells is species to the genus of primate in claims 1-8 and claim 11 or the '806 patent. All other limitations are essentially identical for claims 1-8 and claim 11 as in claims 1-8 and claim 11 of the '806 patent. Thus, the Count anticipates claims 1-8 and claim 11 of the '780 patent, as a species (human) of the genus (primate) and therefore, claims 1-8 and claim 11 should be designated as corresponding to the Count.

Claims 39-44 of the present application do not correspond exactly to the proposed Count, but should still correspond to the Count because if the Count was prior art to the claims, claims 39-44 of the present application would be unpatentable over the Count under 35 U.S.C. 102 or 103. None of the limitations in claims 39-44 of the present application make them patentably

distinct over the Count, which includes claims 4, 37, and 38 of the present application. The limitations of claims 39-44 of the present application merely set forth inherent characteristics shared by the cells of Count. Inherent characteristics do not make a claim separately patentable.

5. Requirement of 37 C.F.R. § 1.607(a)(5)

The terms of claims 37-44, including claims 37 and 38, of the present application identified as corresponding to the count can be applied to Applicant's specification as shown in Appendix II attached hereto.

6. Requirement of 37 C.F.R. § 1.607(a)(6)

i. Claim 4

The Thomson '806 patent issued on March 13, 2001. The 135(b) bar date for the '806 patent is March 13, 2002. The Thompson '637 application was published on January 9, 2003. The 135(b) bar date for the '637 application is January 9, 2004. The Thompson '289 application was published on September 27, 2001. The 135(b) bar date for the '289 application is September 27, 2002. Present claim 4 was amended to its current form on December 20, 2001. This is less than 1 year from the issuance or publication of any of the claims of the '806 patent or the '637 or '289 applications. Insofar as claim 4 of the above-identified application was pending prior to one year after the Thomson '806 patent issued and the Thompson '637 and '289 applications published, the requirements of 35 U.S.C. § 135(b) have been satisfied and are not relevant for claim 4.

For a claim to act as a 135(b) bar it must be for "substantially the same subject matter" as the claim at issue. 35 U.S.C. § 135(b). "Substantially the same subject matter" has been interpreted very narrowly to require that "all material limitations" be present. See, e.g., Parks v. Fine 773 F.2d 1577 (Fed. Cir. 1985) and Corbett v. Chisholm 568 F.2d 769 (C.C.P.A. 1977) (Copies attached). All of claims in the Thompson '780 patent are drawn to primate cells and none of the claims are limited to human cells. Thus, the claims in the '780 patents are not claims for substantially the same subject matter as present claim 4, which is limited to human cells. Accordingly, no 135(b) bar exists.

ii. Claim 37

Claim 37 is the same as originally filed claim 4 with the exception of the recitation of "wherein the cell has a normal karyotype." The phrase "wherein the cell has a normal karyotype" was added to present claim 4 by Amendment on December 20, 2001. Thus, every limitation of claim 37 was pending before the 135(b) bar dates of the Thomson '806 patent and the Thompson '637 and '289 applications. Thomson v. Hamilton 33 C.C.P.A. 732, 735 (C.C.P.A. 1946) (Copy included) held that limitations from multiple claims pending prior to the 135(b) bar date can be combined to overcome a 135(b) bar even if no single claim contained all of the limitations of the potentially barring claim as long as the claims are drawn to similar subject matter. The court stated,

> An examination of these five claims clearly shows that each feature of the counts had been covered by [a] claim. Claims 1 and 2 are more specific than count 1 in that they include the bulged feature above mentioned. Claim 3 was sufficiently broad to read on the Thompson structure and it embodied the essential features in issue. Claim 4, except possibly for the stated method of assembly of the parts, was also sufficiently broad to read on the Thompson disclosure. While it is true that the exact terminology of the counts in issue was not found in the Hamilton application prior to the year period, this is of no consequence as the rule does not require him to make the identical claims of the patent during this period; all that is required is that he shall be urging claims covering the matter which is claimed in the patent before the critical period has terminated.

Id. at 735.

Clearly claim 4 as originally filed and claim 4 as amended, in combination, are drawn to similar subject matter. Thus, consistent with Thomson v. Hamilton, Applicant is allowed to rely on original claim 4 and amended claim 4, both of which were pending before the bar date of March 13, 2002. Thus, no 135(b) bar exists.

All of claims in the Thompson '780 patent are drawn to primate cells and none of the claims are limited to human cells. Thus, the claims in the '780 patents are not claims for

substantially the same subject matter as present claim 37, which is limited to human cells. Accordingly, no 135(b) bar exists.

iii. Claim 38

Claim 38 is the same as originally filed claim 4 which was pending as of the filing of the original application on March 6, 1997. This is before the 135(b) bar dates of the Thomson '806 and '780 patents and the Thompson '637 and '289 applications. Thus, the requirements of 35 U.S.C. § 135(b) have been satisfied and are not relevant for claim 38.

iv. Dependent claims 39-44

Dependent claims 39-41 add a limitation that the cell stains positive for the SSEA-1 antigen and claims 42-44 add the limitations that the cell stains positive for the SSEA-1 antigen and stains positive for alkaline phosphatase. No claim can act as a 135(b) bar for any claim having these limitations because the barring claim must have all material limitations to be barring.

No claim of the '806 or '780 patents or the '637 and '289 applications have the limitation that the cell stains positive for the SSEA-1 antigen. Because no claim can act as a 135(b) bar for claims having the SSEA-1 positive limitation, claims 39-44 are not barred under 135(b) by any claim of the '806 or '780 patents or the '637 and '289 applications.

All of claims in the Thompson '780 patent are drawn to primate cells and none of the claims are limited to human cells. Thus, the claims in the '780 patent are not claims for substantially the same subject matter as present claims 39-44, which are limited to human cells. Accordingly, no 135(b) bar exists.

C. Requirements of 37 C.F.R. § 1.604(a)(1)-(a)(3)

In accordance with 37 C.F.R. § 1.604(a)(1)-(a)(3), Applicant offers the following:

1. Requirement of 37 C.F.R. § 1.604(a)(1)

The proposed count is as follows: Claim 4 of the present application, claim 37 of the present application, or claim 38 of the present application. The text of the proposed count is:

An isolated human pluripotential stem cell which can:

(a) be maintained on feeder layers for at least 20 passages; and

(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture, wherein the cell has a normal karyotype;

or

An isolated human pluripotential embryonic stem cell which can

(a) be maintained on feeder layers for at least 20 passages; and

(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture, wherein the cell has a normal karyotype;

or

An isolated human pluripotential embryonic stem cell which can

(a) be maintained on feeder layers for at least 20 passages; and

(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture.

Claims 4 and 37-44 of the present application correspond to the Count.

2. Requirement of 37 C.F.R. § 1.604(a)(2)

Claims 1-8 and 11 of the '637 and the '289 application correspond to the proposed Count and should be designated as corresponding to the Count. Claim 1 of the '637 application and claim 1 of the '289 application are nearly identical to claim 1 of the '806 patent. As discussed below, claim 1 of the '806 patent and claim 4 of the present application are the same patentable subject matter (see Section D, below, and Appendix III). Claims 2-8 and 11 of the '637 and '289 applications are similar to claims 2-8 and 11 of the '806 and '780 patent and are inherently present and/or obvious in view of the Count for similar reasons (see analysis above in Section B). The face of the published '637 and '289 applications indicated that the applications are assigned to the Wisconsin Alumni Research Foundation.

3. **Requirement of 37 C.F.R. § 1.604(a)(3)**

Claims 1-8 and 11 of the '637 and '289 applications should be designated as corresponding to this Count and an interference should be declared as discussed in Section D, below, and Appendix III. The subject matter of claims 1-8 and 11 of the '637 and '289 applications is nearly identical to the claimed subject matter of the claims in the '806 patent (see Appendix IV) and the claims are inherently anticipated and/or obvious in view of the Count for similar reasons (see analysis above in Section B).

D. Interference in Fact

Although claim 1 of the '806 patent and claim 4 of the present application are not identical there is still interference in fact between them as discussed below.

There is an interference in fact when at least one claim of a party designated to correspond to a count and at least one claim of an opponent that is designated to correspond to the count define the same patentable invention. 37 C.F.R. § 1.601(j). The standard for whether claims define the same patentable invention is found in 37 C.F.R. § 1.601(n). 37 C.F.R. § 1.601(n) states, "Invention "A" is the same patentable invention as an invention "B" when invention "A" is the same as (35 U.S.C. 102) or is obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A". Invention "A" is a separate patentable invention with respect to invention "B" when invention "A" is new (35 U.S.C. 102) and non-obvious (35 U.S.C. 103) in view of invention "B" assuming invention "B" is prior art with respect to invention "A".

The 1.601(n) standard has been interpreted to require a two way test, meaning that invention A must anticipate or make obvious invention B and invention B must anticipate or make obvious invention A. Eli Lilly v. Board of Regents of University of Washington, 334 F.3d 1264, 1268 (Fed. Cir. 2003).

The analysis is similar to an obviousness type double patenting analysis, meaning the claims are used to anticipate or make obvious each other either alone in combination with any

prior art. Prior art can be used to show what the skilled artisan would have known or understood at the time of the claims.

Furthermore as long as at least one claim in a pending application and at least one claim in an issued patent or another pending application meet the standard of 37 C.F.R. § 1.601(n) an interference shall be declared between the interfering application and application/patent. 37 C.F.R. § 1.601(i) and (j).

Claim 1 of the '806 patent and claim 4 of the present application are the same patentable subject matter as defined by their terms and respective specifications. As evidence of this, a side-by-side comparison of these claims is provided in Appendix III attached hereto. The side-by-side comparison appearing in Appendix III shows that each of the claims in question would either anticipate, or at least render obvious, the other. Accordingly, Claim 4 of the present application defines the "same patentable invention" as Claim 1 of the Thomson '806 patent under 37 C.F.R. 1.601(n) as analyzed below.

Claim 4 of the present application is drawn to a "human pluripotential stem cell" which is understood to be a cell that can be maintained without differentiation while retaining the ability to differentiate into many different cell types.[1] Claim 1 of the '806 patent is drawn to a "pluripotent human embryonic stem cell." These two phrases do not make claim 4 of the present application and claim 1 of the '806 patent patentably distinct as they cover significantly overlapping sets of cells. For example, the '806 patent defines an embryonic stem cell at column 3, lines 54-59, as follows:

"True ES cells should: (i) be capable of indefinite proliferation in vitro in an undifferentiated state; (ii) maintain a normal karyotype through prolonged culture; and (iii) maintain the potential to differentiate to derivatives of all three embryonic germ layers (endoderm, mesoderm, and ectoderm) even after prolonged culture."

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[1] While not necessarily dispositive, see the definition of "pluripotent" at the NIH site for Stem cells (defining pluripotent as the "Ability of a single stem cell to develop into many different cell types of the body." (http://stemcells.nih.gov/infoCenter/glossary.asp).

It is clear that "human pluripotential stem cell" and "pluripotent human embryonic stem cell" refer to similar sets of cells. However, should the PTO decide that claim 4 of the present application and claim 1 of the '806 patent are distinct under the two way test of 37 C.F.R. § 1.601(n), it is noted that it would be because "human pluripotential stem cells" is broader than "pluripotent human embryonic stem cells", and that "pluripotent human embryonic stem cells" would be patentably distinct over the genus of "human pluripotential stem cells." In this case, claims to "human pluripotential stem cells" would cover "pluripotent human embryonic stem cells." Nevertheless, the present application discloses pluripotent human embryonic stem cells (p.8, lines 6-8).

Claim 4 of the present application also requires that the cells be "maintained on feeder layers." Claim 1 of the '806 patent requires that the cell be "inhibited from differentiation when cultured on a fibroblast feeder layer." There is no patentable distinction between these two requirements because as of January 20, 1995, those of skill in the art understood that "pluripotential" and "embryonic" stem cells could be maintained on at least "fibroblast feeder layers." Indeed, the present application disclosed using a type of fibroblast feeder layer (p. 15, lines 10-14, for example, where Sl/Sl^4 cell lines, which are a type of fibroblast cell line and are used as feeder layers.) Should the PTO decide that claim 4 of the present application and claim 1 of the '806 patent are distinct under the two way test of 37 C.F.R. § 1.601(n), it is noted that it would be because "feeder layers" is broader than "fibroblast feeder layers", and that "fibroblast feeder layers" would be patentably distinct over the genus of "feeder layers." In this case, claims to "feeder layers" would cover "fibroblast feeder layers."

Claim 4 of the present application also requires that the cells be maintained "for at least 20 passages." Claim 1 of the '806 patent requires that the cells be able to "proliferate in an in vitro culture for over one year." These two requirements are not patentably distinct. Again, the requirement of claim 4 of the present application can be seen as broader than the requirement of claim 1 of the '806 patent because every cell grown for "over one year" will have been "maintained for at least 20 passages." The limitation of "over one year" is not patentably distinct

because the characteristic of "over one year" is an inherent property that does not lend patentability.

Claim 4 of the present application also requires that the cells be able to "give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture." Claim 1 of the '806 patent indicates that the cells "maintain[] the potential to differentiate to derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture." These two requirements are not patentably distinct. Again, while the requirement of claim 4 of the present application is broader than the requirement of claim 1 of the '806 patent, these requirements are not patentably distinct because given claim 4 and that which was known in the art, the further limitations of mesoderm, ectoderm, and endoderm would have been obvious. For example the present application discloses the production of cell types from all three types of tissue, endoderm, mesoderm, and ectoderm. (p. 20, lines 11-21).

Claim 4 of the present application also requires that "the cell has a normal karyotype." The corresponding requirement in claim 1 of the '806 patent is that the cell "maintains a karyotype in which the chromosomes are euploid and not altered through prolonged culture." These requirements are not patentably distinct. "Normal karyotype" would be understood by the skilled artisan to mean that the cells are "euploid."

In conclusion, claim 4 of the present application covers a set of cells that are clearly largely overlapping with the set of cells claimed in claim 1 of the '806 patent. Furthermore, any differences between these claims do not make the claims patentably distinct over one another. It is true that claim 4 of the present application can be seen as a genus claim to the sub-genus of claim 1 of the '806 patent, but in the two way patentability test set forth in Eli Lilly, claim 1 of the '806 patent would anticipate or render obvious claim 4 of the present application in the first part of the two way analysis. In the second part of the two way analysis, claim 4 would either anticipate or make obvious claim 1 of the '806 patent because any differences between claim 1 of the '806 patent and claim 4 of the present application would have been obvious in view of claim 4 and the present application.

Thus, Applicant requests that an interference be declared between the present application and at least the Thomson '806 and '780 patents and the Thompson '637 and '289 applications as there is an interference in fact as set forth in 37 C.F.R. § 1.601(j) between at least claim 4 of the present application and claim 1 of the '806 patent.

E. Benefit

Applicant hereby requests benefit of the effective filing date of at least Application No. 08/217,921 ('921 application) which was filed on filed March 6, 1997. The '921 application was 37 C.F.R 1.60 continuation of the '921 application, which was filed on March 25, 1994, Therefore applicants also request benefit of the effective filing date of March 25, 1994 of Application no. 08/217,921. The '921 application is also a continuation-in-part of Application No. 07/958,562, ('562 application) filed on October 8, 1992. Therefore, Applicant also requests benefit of Application No. 07/958,562, filed Oct. 8, 1992. Thus, in the declaration of interference Applicant requests the benefit of Application Nos. 08/217,921 and 07/958,562, as evidenced by the disclosure in Applicant's prior applications[2].

Applicant is entitled to benefit of their earlier filed applications for purposes of this interference if the Count reads on at least one adequately disclosed embodiment in the earlier application. Weil v. Fritz, 572 F.2d 856, 865-66 n.16, 196 USPQ 600, 608 n.16 (CCPA 1978). The present application is a continuation of Application No. 08/217,921 filed March 25, 1994, and thus, that which is supported in the present application, as set out in Appendix II is supported in Application No. 08/217,921 at the same places. Because the present application discloses an embodiment of the Count, the '921 application also discloses an embodiment of the Count (see Appendix II). Therefore, Applicant should be accorded at least the benefit of this application.

Furthermore, the present application claims priority to Application No. 08/217,921 which is a continuation-in-part of Application No. 07/958,562, filed October 8, 1992, now issued as

[2] This application claims priority to and is a continuation of Application No. 08/217,921 filed March 25, 1994, which itself claims priority to and is a continuation-in-part of and divisional of Application No. 07/958,562, filed October 8, 1992, now issued as U.S. Patent 5,453,357.

U.S. Patent 5,453,357. Evidence of support in the '562 application for Applicant's claims and the Count is provided in Appendix II to this request. Appendix II shows where support for Applicant's claims and the Count can be found in the earliest priority application.

As discussed and agreed to in the interview with Examiner Woitach on October 20, 2003, the method for producing pluripotential stem cells and pluripotential embryonic stem cells disclosed and enabled in the present application is the same method that is described in the original priority application, Application No. 07/598,562, filed on October 8, 1992, now U.S. patent 5,453,357. Therefore, Applicant is entitled to full benefit of the '562 application, as well as benefit of the '921 application.

F. Requirements of 37 C.F.R. § 1.608

As to the requirements of 37 C.F.R. § 1.608, both of the effective filing dates, i.e., March 25, 1994 and October 8, 1992, of the present application are **earlier** than the earliest possible priority date of the '806 patent, the '780 patent, the '637 application, and the '289 application, which is January 20, 1995. It is noted that there is at least one intervening continuation-in-part in the chain of priority for the '806 and '780 patents and the '637 and '289 applications. Accordingly, Applicant submits that no showing under 37 C.F.R. § 1.608 is required.

G. Party Designation

In light of the fact that Applicant's effective filing date is earlier than the earliest possible priority date for the Thomson '806 patent, Applicant should be designated as the senior party in the interference.

As a final matter, should the Examiner have any questions regarding this paper, or the application in general, he is invited to telephone the undersigned at his earliest convenience. No fee is believed due. However, the Commissioner is hereby authorized to charge any fees that may be required to the Deposit Account No. 14-0629.

A Credit Card Payment Form PTO-2038 authorizing payment in the amount of $1125.00, representing $740.00 for the fee for a small entity under 37 C.F.R. § 1.17(a)(4) and $385.00 for the fee for a small entity under 37 C.F.R. § 1.17(e), an Amendment And Response To Office Action, a Supplemental Information Disclosure Statement, a Request For Interference Pursuant To 37 C.F.R. §§ 1.604 And 1.607, and a Request For a Four-Month Extension Of Time are enclosed. This amount is believed to be correct; however, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 14-0629.

Respectfully submitted,

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CERTIFICATE OF EXPRESS MAILING UNDER 37 C.F.R. § 1.10

I hereby certify that this correspondence, including any items indicated as attached or included, is being deposited with the United States Postal Service as Express Mail, Label No. El 9920 18835 US, in an envelope addressed to: Mail Stop RCE, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450, on the date indicated below.

Phillip A. Van Gelder — June 1, 2004
Phillip A. Van Gelder — Date

APPENDIX I - CLAIMS PENDING AFTER ENTRY OF AMENDMENT FILED WITH THIS REQUEST

4. An isolated human pluripotential stem cell which can (a) be maintained on feeder layers for at least 20 passages; and (b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture, wherein the cell has a normal karyotype.
37. An isolated human pluripotential embryonic stem cell which can (a) be maintained on feeder layers for at least 20 passages; and (b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture, wherein the cell has a normal karyotype.
38. An isolated human pluripotential embryonic stem cell which can (a) be maintained on feeder layers for at least 20 passages; and (b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture.
39. The cell of claim 4, wherein the cell stains positive for the SSEA-1 antigen.
40. The cell of claim 37, wherein the cell stains positive for the SSEA-1 antigen.
41. The cell of claim 38, wherein the cell stains positive for the SSEA-1 antigen.
42. The cell of claim 4, wherein the cell stains positive for the SSEA-1 antigen and stain positive for alkaline phosphatase.
43. The cell of claim 37, wherein the cell stains positive for the SSEA-1 antigen and stain positive for alkaline phosphatase.
44. The cell of claim 38, wherein the cell stains positive for the SSEA-1 antigen and stain positive for alkaline phosphatase.

APPENDIX II - 37 C.F.R. 1.607(A)(5) ANALYSIS

Applicant's New Claim	Supporting Disclosure In Application
37. An isolated human pluripotential embryonic stem cell which can	'829 application (present) and the '921 application -- page 22, lines 29-30 "Method for the isolation of pluripotential stem cells from human primordial germ cells and human embryonic (fetal) gonads" '592 application – page 9, lines 7-8 " Mammalian ES cells such as rats, rabbits, guinea pigs, goats, pigs, cows, and humans can all be obtained." '829 application (present) and the '921 application -- page 8, lines 6-12, "A "pluripotential embryonic stem cell" as used herein means a cell which can give rise to many differentiated cell types in an embryo or adult, including the germ cells (sperm and eggs). Pluripotent embryonic stem cells are also capable of self-renewal. Thus, these cells not only populate the germ line and give rise to a plurality of terminally differentiated cells which comprise the adult specialized organs, but also are able to regenerate themselves. This cell type is also referred to as an "ES cell" herein." '592 application – page 8, lines 7-11 "A "pluripotential embryonic stem cell" as used herein means a cell which can give rise to many differentiated cell types in an embryo or adult, including the germ cells (sperm and eggs).
(a) be maintained on feeder layers for at least 20 passages; and	'829 application (present) and the '921 application -- page 4, lines 3-5, '592 application – page 4, lines 5-6 "The present invention provides a non-mouse, including human, pluripotential embryonic stem cell which can: (a) be maintained on feeder layers for at least 20 passages; and"

(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture,	'829 application (present) and the '921 application -- page 4, lines 6-7, '592 application – page 4, lines 7-8 "(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture."
wherein the cell has a normal karyotype.	'829 application (present) and the '921 application -- page 19, lines 17-20, '592 application –page 17, lines 15-19 "Two independent lines at passage 14 (1/14, 2/14) and one at passage 20 (3/20) were karyotyped. Most cells had a normal or near normal XY karyotype, but in two lines (2/14 and 3/20) there was a significant proportion of trisomic cells."
38. An isolated human pluripotential embryonic stem cell which can	'829 application (present) and the '921 application -- page 22, lines 29-30, "Method for the isolation of pluripotential stem cells from human primordial germ cells and human embryonic (fetal) gonads" '592 application – page 9, lines 7-8 " Mammalian ES cells such as rats, rabbits, guinea pigs, goats, pigs, cows, and humans can all be obtained." '829 application (present) and the '921 application -- page 8, lines 6-12, "A "pluripotential embryonic stem cell" as used herein means a cell which can give rise to many differentiated cell types in an embryo or adult, including the germ cells (sperm and eggs). Pluripotent embryonic stem cells are also capable of self-renewal. Thus, these cells not only populate the germ line and give rise to a plurality of terminally differentiated cells which comprise the adult specialized organs, but also are able to regenerate themselves. This cell type is also referred to as an "ES cell" herein." '592 application – page 8, lines 7-11 "A "pluripotential embryonic stem cell" as used herein means a cell which can give rise to many differentiated cell types in an embryo or adult, including the germ cells (sperm and eggs).

(a) be maintained on feeder layers for at least 20 passages; and	'829 application (present) and the '921 application -- page 4, lines 3-5, '592 application – page 4, lines 5-6 "The present invention provides a non-mouse, including human, pluripotential embryonic stem cell which can: (a) be maintained on feeder layers for at least 20 passages; and"
(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture.	'829 application (present) and the '921 application -- page 4, lines 6-7, '592 application – page 4, lines 7-8 "(b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture."
39. The cell of claim 4, wherein the cell stains positive for the SSEA-1 antigen.	'829 application (present) and the '921 application -- page 18, lines 28-31, '592 application – page 16, lines 24-28 "These colonies are also positive for the expression of the antigen SSEA-1, a characteristic of PGCs (Donovan et al., 1986) and undifferentiated embryonal carcinoma and ***ES*** cells (Solter and Knowles, 1978) (FIG. 2G, H)."
40. The cell of claim 37, wherein the cell stains positive for the SSEA-1 antigen.	'829 application (present) and the '921 application -- page 18, lines 28-31, '592 application – page 16, lines 24-28 "These colonies are also positive for the expression of the antigen SSEA-1, a characteristic of PGCs (Donovan et al., 1986) and undifferentiated embryonal carcinoma and ***ES*** cells (Solter and Knowles, 1978) (FIG. 2G, H)."
41. The cell of claim 38, wherein the cell stains positive for the SSEA-1 antigen.	'829 application (present) and the '921 application -- page 18, lines 28-31, '592 application – page 16, lines 24-28 "These colonies are also positive for the expression of the antigen SSEA-1, a characteristic of PGCs (Donovan et al., 1986) and undifferentiated embryonal carcinoma and ***ES*** cells (Solter and Knowles, 1978) (FIG. 2G, H)."
42. The cell of claim 4, wherein the cell stains positive for the SSEA-1 antigen and stains positive for alkaline phosphatase.	'829 application (present) and the '921 application -- page 18, lines 26-31, '592 application – page 16, lines 21-28 "By day 6 in secondary culture, large colonies of densely packed AP positive cells resembling embryonic stem (***ES***) cells are present (FIG. 2D, E; FIG. 4, A), with an overall plating efficiency of about 5%. These colonies are also positive for the expression of the antigen SSEA-1, a characteristic of PGCs (Donovan et al., 1986) and undifferentiated embryonal carcinoma and ***ES*** cells (Solter and Knowles, 1978) (FIG. 2G, H)."

43. The cell of claim 37, wherein the cell stains positive for the SSEA-1 antigen and stains positive for alkaline phosphatase.	'829 application (present) and the '921 application -- page 18, lines 26-31, '592 application – page 16, lines 21-28 "By day 6 in secondary culture, large colonies of densely packed AP positive cells resembling embryonic stem (***ES***) cells are present (FIG. 2D, E; FIG. 4, A), with an overall plating efficiency of about 5%. These colonies are also positive for the expression of the antigen SSEA-1, a characteristic of PGCs (Donovan et al., 1986) and undifferentiated embryonal carcinoma and ***ES*** cells (Solter and Knowles, 1978) (FIG. 2G, H)."
44. The cell of claim 38, wherein the cell stains positive for the SSEA-1 antigen and stains positive for alkaline phosphatase.	'829 application (present) and the '921 application -- page 18, lines 26-31, '592 application – page 16, lines 21-28 "By day 6 in secondary culture, large colonies of densely packed AP positive cells resembling embryonic stem (***ES***) cells are present (FIG. 2D, E; FIG. 4, A), with an overall plating efficiency of about 5%. These colonies are also positive for the expression of the antigen SSEA-1, a characteristic of PGCs (Donovan et al., 1986) and undifferentiated embryonal carcinoma and ***ES*** cells (Solter and Knowles, 1978) (FIG. 2G, H)."

APPENDIX III - COMPARISON OF CLAIM 4 AND THOMPSON CLAIM 1

Applicant's Claim 4	'806 Claim 1 and Related Disclosure In Thomson '806 Patent
4A) An isolated human pluripotential stem cell which can	1A) A purified preparation of pluripotent human embryonic stem cells which
4B) (a) be maintained on feeder layers	1B) (iv) is inhibited from differentiation when cultured on a fibroblast feeder layer.
4C) for at least 20 passages; and	1C) (i) will proliferate in an in vitro culture for over one year,
4D) (b) give rise to embryoid bodies and multiple differentiated cell phenotypes in monolayer culture,	1D) (iii) maintains the potential to differentiate to derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and
4E) wherein the cell has a normal karyotype.	1E) ii) maintains a karyotype in which the chromosomes are euploid and not altered through prolonged culture,

APPENDIX IV PENDING OR ISSUED CLAIMS IN '637 AND '289 APPLICATIONS AND '806 AND '780 PATENT

6,200,806	5,843,780	09/982,637	09/761,289
1. A purified preparation of pluripotent human embryonic stem cells which (i) will proliferate in an in vitro culture for over one year, (ii) maintains a karyotype in which the chromosomes are euploid and not altered through prolonged culture, (iii) maintains the potential to differentiate to derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (iv) is inhibited from differentiation when cultured on a fibroblast feeder layer.	1. A purified preparation of primate embryonic stem cells which (i) is capable of proliferation in an in vitro culture for over one year, (ii) maintains a karyotype in which all the chromosomes characteristic of the primate species are present and not noticeably altered through prolonged culture, (iii) maintains the potential to differentiate into derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and(iv) will not differentiate when cultured on a fibroblast feeder layer.	1. A purified preparation of human embryonic stem cells which (i) is capable of proliferation in an in vitro culture for over one year, (ii) maintains a karyotype in which all the chromosomes characteristic of the human species are present and not noticeably altered through prolonged culture, (iii) maintains the potential to differentiate to derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (iv) are inhibited from differentiation when cultured on a fibroblast feeder layer.	1. A purified preparation of human embryonic stem cells which (i) is capable of proliferation in an in vitro culture for over one year, (ii) maintains a karyotype in which all the chromosomes characteristic of the human species are present and not noticeably altered through prolonged culture, (iii) maintains the potential to differentiate to derivatives of endoderm, mesoderm, and ectoderm tissues throughout the culture, and (iv) are inhibited from differentiation when cultured on a fibroblast feeder layer.
2. The preparation of claim 1, wherein the stem cells will spontaneously differentiate to trophoblast and produce chorionic gonadotropin when cultured to high density.	2. The preparation of claim 1 wherein the stem cells will spontaneously differentiate to trophoblast and produce chorionic gonadotropin when cultured to high density.	2. The preparation of claim 1, wherein the stem cells will spontaneously differentiate to trophoblast and produce chorionic gonadotropin when cultured to high density.	2. The preparation of claim 1, wherein the stem cells will spontaneously differentiate to trophoblast and produce chorionic gonadotropin when cultured to high density.

3. A purified preparation of pluripotent human embryonic stem cells wherein the cells are negative for the SSEA-1 marker, positive for the SSEA-4 marker, express alkaline phosphatase activity, are pluripotent, and have euploid karyotypes and in which none of the chromosomes are altered.	3. A purified preparation of primate embryonic stem cells wherein the cells are negative for the SSEA-1 marker, positive for the SSEA-3 marker, positive for the SSEA-4 marker, express alkaline phosphatase activity, are pluripotent, and have karyotypes which includes the presence of all of the chromosomes characteristic of the primate species and in which none of the chromosomes are noticeably altered.	3. A purified preparation of human embryonic stem cells wherein the cells are essentially negative for the SSEA-1 marker, positive for the SSEA-4 marker, express alkaline phosphatase activity, are pluripotent, and have karyotypes which includes the presence of all of the chromosomes characteristic of the human species and in which none of the chromosomes are noticeably altered.	3. A purified preparation of human embryonic stem cells wherein the cells are essentially negative for the SSEA-1 marker, positive for the SSEA-4 marker, express alkaline phosphatase activity, are pluripotent, and have karyotypes which includes the presence of all of the chromosomes characteristic of the human species and in which none of the chromosomes are noticeably altered.
4. The preparation of claim 3, wherein the cells are positive for the TRA-1-60, and TRA-1-81 markers.	4. The preparation of claim 3 wherein the cells are positive for the TRA-1-60, and TRA-1-81 markers.	4. The preparation of claim 3, wherein the cells are positive for the TRA-1-60, and TRA-1-81 markers.	4. The preparation of claim 3, wherein the cells are positive for the TRA-1-60, and TRA-1-81 markers.
5. The preparation of claim 3, wherein the cells continue to proliferate in an undifferentiated state after continuous culture for at least one year.	5. The preparation of claim 3 wherein the cells continue to proliferate in an undifferentiated state after continuous culture for at least one year.	5. The preparation of claim 3, wherein the cells continue to proliferate in an undifferentiated state after continuous culture for at least one year.	5. The preparation of claim 3, wherein the cells continue to proliferate in an undifferentiated state after continuous culture for at least one year.
6. The preparation of claim 3, wherein the cells will differentiate to trophoblast when cultured beyond confluence and will produce chorionic gonadotropin.	6. The preparation of claim 3 wherein the cells will differentiate to trophoblast when cultured beyond confluence and will produce chorionic gonadotropin.	6. The preparation of claim 3, wherein the cells will differentiate to trophoblast when cultured beyond confluence and will produce chorionic gonadotropin.	6. The preparation of claim 3, wherein the cells will differentiate to trophoblast when cultured beyond confluence and will produce chorionic gonadotropin.
7. The preparation of claim 3, wherein the cells remain euploid for more than one year of continuous culture.	7. The preparation of claim 3 wherein the cells remain euploid for more than one year of continuous culture.	7. The preparation of claim 3, wherein the cells remain euploid for more than one year of continuous culture.	7. The preparation of claim 3, wherein the cells remain euploid for more than one year of continuous culture.

8. The preparation of claim 3, wherein the cells differentiate into cells derived from mesoderm, endoderm and ectoderm germ layers when the cells are injected into a SCID mouse.	8. The preparation of claim 3 wherein the cells differentiate into cells derived from mesoderm, endoderm and ectoderm germ layers when the cells are injected into a SCID mouse.	8. The preparation of claim 3, wherein the cells differentiate into cells derived from mesoderm, endoderm and ectoderm germ layers when the cells are injected into a SCID mouse.	8. The preparation of claim 3, wherein the cells differentiate into cells derived from mesoderm, endoderm and ectoderm germ layers when the cells are injected into a SCID mouse.
9. A method of isolating a pluripotent human embryonic stem cell line, comprising the steps of: (a) isolating a human blastocyst; (b) isolating cells from the inner cell mass of the blastocyte of (a); (c) plating the inner cell mass cells on embryonic fibroblasts, wherein inner cell mass-derived cell masses are formed; (d) dissociating the mass into dissociated cells; (e) replating the dissociated cells on embryonic feeder cells; (f) selecting colonies with compact morphologies and cells with high nucleus to cytoplasm ratios and prominent nucleoli; and (g) culturing the cells of the selected colonies to thereby obtain an isolated pluripotent human embryonic stem cell line.	9. A method of isolating a primate embryonic stem cell line, comprising the steps of: (a) isolating a primate blastocyst; (b) isolating cells from the inner cell mass of the blastocyst of (a); (c) plating the inner cell mass cells on embryonic fibroblasts, wherein inner cell mass-derived cells masses are formed; (d) dissociating the mass into dissociated cells; (e) replating the dissociated cells on embryonic feeder cells; (f) selecting colonies with compact morphologies and cells with high nucleus to cytoplasm ratios and prominent nucleoli; and (g) culturing the cells of the selected colonies.	9. A method of isolating a human embryonic stem cell line, comprising the steps of: (a) isolating a human blastocyst; (b) isolating cells from the inner cell mass of the blastocyte of (a); (c) plating the inner cell mass cells on embryonic fibroblasts, wherein inner cell mass-derived cell masses are formed; (d) dissociating the mass into dissociated cells; (e) replating the dissociated cells on embryonic feeder cells; (f) selecting colonies with compact morphologies and cells with high nucleus to cytoplasm ratios and prominent nucleoli; and (g) culturing the cells of the selected colonies.	9. A method of isolating a human embryonic stem cell line, comprising the steps of: (a) isolating a human blastocyst; (b) isolating cells from the inner cell mass of the blastocyte of (a); (c) plating the inner cell mass cells on embryonic fibroblasts, wherein inner cell mass-derived cell masses are formed; (d) dissociating the mass into dissociated cells; (e) replating the dissociated cells on embryonic feeder cells; (f) selecting colonies with compact morphologies and cells with high nucleus to cytoplasm ratios and prominent nucleoli; and (g) culturing the cells of the selected colonies.
10. A method as claimed in claim 9, further comprising maintaining the isolated cells on a fibroblast feeder layer to prevent differentiation.	10. A method as claimed in claim 9 further comprising maintaining the isolated cells on a fibroblast feeder layer to prevent differentiation.	10. A method as claimed in claim 9, further comprising maintaining the isolated cells on a fibroblast feeder layer to prevent differentiation.	10. A method as claimed in claim 9, further comprising maintaining the isolated cells on a fibroblast feeder layer to prevent differentiation.
11. A cell line developed by the method of claim 9.	11. A cell line developed by the method of step 9.	11. A cell line developed by the method of step 9.	